WHAT IS CLAIMED IS:

1. A method of assessing the effect of a test condition on G-protein-coupled receptor (GPCR) pathway activity, comprising:

a) providing a cell that expresses a GPCR as a fusion protein to one mutant form of reporter enzyme and an interacting protein partner as a fusion to another mutant form of enzyme,

wherein said cell also expresses an arrestin, wherein said arrestin is modified to enhance binding of said arrestin to said GPCR, wherein said enhanced binding between said arrestin and said GPCR increases sensitivity of detection of said effect of said test condition;

b) exposing the cell to a ligand for said GPCR under said test condition; and

c) monitoring activation of said GPCR by complementation of said reporter enzyme;

wherein increased reporter enzyme activity in the cell compared to that which occurs in the absence of said test condition indicates increased GPCR interaction with its interacting protein partner compared to that which occurs in the absence of said test condition, and decreased reporter enzyme activity in the cell compared to that which occurs in the absence of said test condition indicates decreased GPCR interaction with its interacting protein partner compared to that which occurs in the absence of said test condition.

2. A method of assessing the effect of a test condition on G-protein-coupled receptor (GPCR) pathway activity, comprising:

a) providing a cell that expresses a GPCR as a fusion protein to one mutant

form of reporter enzyme and an interacting protein partner as a fusion to another mutant form of enzyme;

wherein said GPCR fusion protein is modified to include one or more sets of serine/threonine clusters, wherein said one or more sets of serine/threonine clusters enhance binding of said GPCR to arrestin, wherein said enhanced binding between said GPCR and said arrestin increases sensitivity of detection of said effect of said test condition;

b) exposing the cell to a ligand for said GPCR under said test condition; and

c) monitoring activation of said GPCR by complementation of said reporter enzyme;

wherein increased reporter enzyme activity in the cell compared to that which occurs in the absence of said test condition indicates increased GPCR interaction with said interacting protein partner compared to that which occurs in the absence of said test condition, and decreased reporter enzyme activity in the cell compared to that which occurs in the absence of said test condition indicates decreased GPCR interaction with interacting protein partner compared to that which occurs in the absence of said test condition.

3. A DNA molecule comprising a sequence encoding a biologically active hybrid GPCR, wherein said hybrid GPCR comprises a GPCR as a fusion protein to one mutant form of reporter enzyme and wherein said hybrid GPCR is modified to include one or more sets of serine/threonine clusters, wherein said one or more sets of serine/threonine clusters enhance binding of said hybrid GPCR to arrestin.

4. A DNA construct capable of directing the expression of a biologically

active hybrid GPCR in a cell, comprising the following operatively linked elements:

a promoter; and

a DNA molecule comprising a sequence encoding a biologically active hybrid GPCR, wherein said hybrid GPCR comprises a GPCR as a fusion protein to one mutant form of reporter enzyme and wherein said hybrid GPCR is modified to include one or more sets of serine/threonine clusters, wherein said one or more sets of serine/threonine clusters enhance binding of said hybrid GPCR to arrestin.

5. A cell transformed with a DNA construct capable of expressing a biologically active hybrid GPCR in a cell, comprising the following operatively linked elements:

a promoter; and

a DNA molecule comprising a sequence encoding a biologically active hybrid GPCR, wherein said hybrid GPCR comprises a GPCR as a fusion protein to one mutant form of reporter enzyme and wherein said hybrid GPCR is modified to include one or more sets of serine/threonine clusters, wherein said one or more sets of serine/threonine clusters enhance binding of said hybrid GPCR to arrestin.

6. A DNA molecule comprising a sequence encoding a biologically active hybrid arrestin, wherein said hybrid arrestin comprises an arrestin as a fusion to one mutant form of reporter enzyme and wherein said hybrid arrestin is modified to enhance binding of said arrestin to GPCR.

7. A DNA construct capable of directing the expression of a biologically active hybrid arrestin in a cell, comprising the following operatively linked

elements:

a promoter; and

a DNA molecule comprising a sequence encoding a biologically active hybrid arrestin, wherein said hybrid arrestin comprises an arrestin as a fusion to one mutant form of reporter enzyme and wherein said hybrid arrestin is modified to enhance binding of said arrestin to GPCR.

8. A cell transformed with a DNA construct capable of expressing a biologically active hybrid arrestin in a cell, comprising the following operatively linked elements:

a promoter; and

a DNA molecule comprising a sequence encoding a biologically active hybrid arrestin, wherein said hybrid arrestin comprises an arrestin as a fusion to one mutant form of reporter enzyme and wherein said hybrid arrestin is modified to enhance binding of said arrestin to GPCR.

9. A method of assessing the effect of a test condition on G-protein-coupled receptor (GPCR) pathway activity, comprising:

a) providing a cell that expresses a GPCR as a fusion protein to one mutant form of reporter enzyme and an interacting protein partner as a fusion to another mutant form of enzyme,

wherein said cell also expresses an arrestin, wherein said arrestin is modified by introducing a point mutation in a phosphorylation-recognition domain to remove a requirement for phosphorylation of said GPCR for arrestin binding to permit binding of said arrestin to said GPCR in said cell regardless of whether said

GPCR is phosphorylated,

b) exposing the cell to a ligand for said GPCR under said test condition; and

c) monitoring activation of said GPCR by complementation of said reporter enzyme;

wherein increased reporter enzyme activity in the cell compared to that which occurs in the absence of said test condition indicates increased GPCR interaction with its interacting protein partner compared to that which occurs in the absence of said test condition, and decreased reporter enzyme activity in the cell compared to that which occurs in the absence of said test condition indicates decreased GPCR interaction with its interacting protein partner compared to that which occurs in the absence of said test condition.

10. The method of Claim 9, wherein said arrestin is mutated to increase a property selected from affinity and avidity for activated, non-phosphorylated GPCR.

11. The method of Claim 10, wherein said arrestin is β-arrestin2 and wherein said β-arrestin2 is mutated to convert Arg169 to an oppositely charged residue.

12. The method of Claim 11, wherein said oppositely charged residue is selected from the group consisting of histidine, tyrosine, phenylalanine and threonine.

13. The method of Claim 9, wherein said arrestin is mutated to increase a property selected from affinity and avidity for activated and phosphorylated GPCR.

14. A method of assessing the effect of a test condition on G-protein-

coupled receptor (GPCR) pathway activity, comprising:

a) providing a cell that expresses a GPCR as a fusion protein to one mutant form of reporter enzyme and an interacting protein partner as a fusion to another mutant form of enzyme;

wherein said GPCR fusion protein is modified to include one or more sets of serine/threonine clusters, said one or more serine/threonine clusters defined as serine or threonine residues occupying three consecutive or three out of four positions in a carboxyl-termini of said GPCR, wherein said one or more sets of serine/threonine clusters enhance binding of said GPCR to arrestin, wherein said enhanced binding between said GPCR and said arrestin increases sensitivity of detection of said effect of said test condition;

b) exposing the cell to a ligand for said GPCR under said test condition; and

c) monitoring activation of said GPCR by complementation of said reporter enzyme;

wherein increased reporter enzyme activity in the cell compared to that which occurs in the absence of said test condition indicates increased GPCR interaction with said interacting protein partner compared to that which occurs in the absence of said test condition, and decreased reporter enzyme activity in the cell compared to that which occurs in the absence of said test condition indicates decreased GPCR interaction with interacting protein partner compared to that which occurs in the absence of said test condition.

15. The method of Claim 1, wherein said modified arrestin exhibits enhanced binding to activated, phosphorylated GPCR.

16. The method of Claim 14, wherein said modified arrestin comprises conversion of Arg169 to an amino acid selected from the group consisting of histidine, tyrosine, phenylalanine and threonine.

17. The method of Claim 14, wherein said modified arrestin comprises conversion of Val170 to alanine.

18. The method of Claim 14, wherein said arrestin is selected from the group consisting of β-arrestin1 and β-arrestin2, and wherein said β-arrestin1or said β-arrestin2 is truncated for all or part of a carboxyl-terminal half of said β-arrestin1 or said β-arrestin2.

19. The method of Claim 18, wherein said β-arrestin1 or said β-arrestin2 is truncated from amino acid 190 of said β-arrestin1 or said β-arrestin2 to said carboxyl-terminal end of said β-arrestin1 or said β-arrestin2.

20. The method of Claim 14, wherein said arrestin is a chimera of β-arrestin1, β-arrestin2 and/or visual arrestin.

21. The method of Claim 10, wherein said arrestin is a chimera of β-arrestin1, β-arrestin2 and/or visual arrestin.

22. The method of Claim 11, wherein said arrestin is a chimera of β-arrestin1, β-arrestin2 and/or visual arrestin.

23. The method of Claim 12, wherein said arrestin is a chimera of β-arrestin1, β-arrestin2 and/or visual arrestin.

24. The method of Claim 10, wherein said arrestin is β-arrestin1 and wherein said β-arrestin2 is mutated to convert Arg170 to an oppositely charged residue.

25. The method of Claim 14, wherein said modified arrestin comprises conversion of Arg170 to an amino acid selected from the group consisting of histidine, tyrosine, phenylalanine and threonine.

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